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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,250	10/28/2005	Zaihui Zhang	540057.414USPC	5096

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EXAMINER	
THOMAS, TIMOTHY P	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
11/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,250	ZHANG ET AL.	
	Examiner	Art Unit	
	Timothy P. Thomas	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,40,42,43 and 45-77* is/are pending in the application.

4a) Of the above claim(s) *1,48,50-53,56-63,66-70 and 72-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40,42,43,45-47,49,54,55,64,65,71 and 77* is/are rejected.

7)☐ Claim(s) [redacted] is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

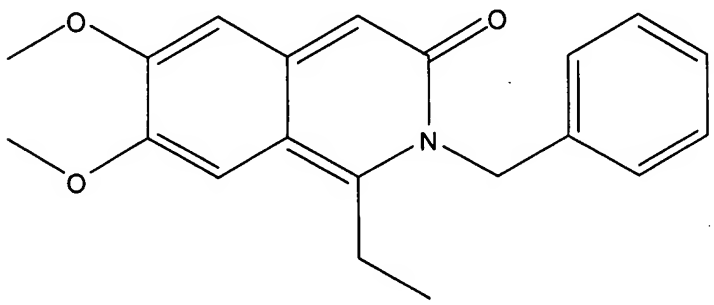
1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/28/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *corrected PTO-892 form*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II (claims 40, 42-43, 45-52 and 54-77 (in part)) in the reply filed on 9/27/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Applicant's election of 2-benzyl-1-ethyl-6,7-dimethoxy-2H-isoquinoline-3-one as the compound of formula (I), which has the following structure:



with the identification that claims 1, 40, 42-43, 45-53, 54-55, 64-65, 71 and 77 read on this compound specie; the in vivo method of treating a mammal of claim 45; and inflammation as the single disclosed disease or disorder in the reply filed on 9/27/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claim 1 and the portions of claims 54-77 that are drawn to a pharmaceutical composition are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

4. Claims 48, 50-53, 56-63, 66-70, and 72-76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim.

Corrected Form

5. The Notice of References Cited, PTO-892, mailed with the Restriction and Election Requirement on 8/28/2007 inadvertantly contained a reference to an incorrect patent number, which has been lined out on the copy submitted with this action. No additional PTO-892 citation of the Kreighbaum, et al. patent (US 4,015,006) is necessary, because the citation appears on the Information Disclosure Statement filed 10/28/2005.

Specification

6. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Isoquinoline-3-one Compounds and Methods for Treating Cancer and Inflammation.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 40, 42-43, 45-47, 49, 54-55, 64-65, 71 and 77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of SGKalpha activity *in vitro* and for methods to assay markers associated with inflammation, does not reasonably provide enablement for a method to treat (which includes "preventing") inflammation or to treat any disorder or condition associated with hyperproliferation or to treat **any** disease (even those that are not associated with inflammation and/or angiogenesis). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has given the term "treating" a special definition that includes both "**prevention** of disease and treatment of pre-existing conditions" (specification, p. 16, 2nd paragraph). To **prevent** a disease or condition implies that the disease/condition will **not** develop, not just to reduce some of the symptoms associated with, or to slow the progression of, or to delay the onset of the disease/condition. Applicant has provided no evidence in support of the claim that inflammation will **not** occur

(prevention). Considering that the elected method of treating inflammation includes the **prevention** of inflammation (or any of the non-elected diseases and conditions) by administration of the elected compound (or any other compound of formula (I)), applicant has not provided enablement for one of ordinary skill in the art to **prevent** inflammation (or any other condition disclosed) from occurring.

It is also not clear that the method will be effective for treating (in the sense of treatment of the pre-existing condition) **any** disorder or condition associated with hyperproliferation and cell survival (claim 45). Such conditions are complex and have different etiologies and pharmaceutical agents for one may not be effective for another conditions. Undue experimentation would be required to determine which compound, if any, of formula (I) would be efficacious for each condition, and what conditions are required and/ or what additional active agents would be necessary for each condition.

Additionally, the broadest reasonable interpretation of claim 47 implies that administration of any compound of formula (I) will be effective to treat **any** preexisting disease or condition and to prevent **any** disease/condition, such as preventing cancer, reversing the progression of Alzheimer's disease, lowering the blood sugar of a type 1 diabetic patient as well as the prevention of inflammation, even in the case of an infection or injury when inflammation normally plays an important role in the healing process. Applicant has not enabled the treatment or prevention of any disease in which inflammation or angiogenesis is not involved.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation,

such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a method of treating (preventing or treating pre-existing) cancer, inflammation or a hyperproliferative disorder (claim 40); a method of treating a mammal having a disorder or condition associated with hyperproliferation and cell survival (claim 45); or a method of treating a mammalian cell (claim 47) by the administration of an effective amount of a compound of formula (I). Thus, the claims taken together with the specification imply that cancer, inflammation, arthritis, or even **any** disease or condition (even those not associated with hyperproliferation or cell survival; e.g., diabetes, heart disease, Alzheimer's disease, cleft palate, autism, etc.) is preventable and treatable by administration of any one of the undeterminably large number of possible compounds embraced by formula (I).

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Costa, et al. ("Angiogenesis and chronic inflammation: cause or consequence?" 2007; Angiogenesis 10:149-166) have reviewed a number of disorders where the association between angiogenesis and inflammation play significant roles. Costa

teaches inflammation is a complex process highly coordinated by pro- and anti-inflammatory molecules that regulate cell chemotaxis, migration and proliferation, which generally ends up in a healing process, although when not properly ordered, the result is persistent inflammation, which can mediate a wide variety of diseases (Introduction); an overview of the complicated processes of inflammation and angiogenesis and the signaling between the two is presented (pp. 149-152). Costa reviews some of the conditions where the two processes play an important role; some of the comments for the first three of these conditions follow: with different with respect to psoriasis, the author has concluded, "a careful appreciation of the involved mechanisms must be provided...it would be better to clearly define the complex interaction between chronic inflammation and angiogenesis in psoriatic lesions prior to developing future therapeutic approaches" (p. 153 end of 1st paragraph); with respect to rheumatoid arthritis, none of the primarily used drugs is curative and all have significant side-effects (p. 153, last paragraph); with respect to osteoarthritis, anti-inflammatory agents are promising approaches, but their application remains in its infancy (top paragraph , p. 155). It is clear that one drug will not cure or even effectively treat all of the conditions associated with inflammation, let alone other diseases and conditions, where inflammation and/or angiogenesis have not been demonstrated to play a significant role (within the scope of instant claim 47).

(5) The relative skill of those in the art:

The relative skill in the art is high.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for inhibition of SGK2alpha activity and some assays to measure effects of inflammation.

However, the specification does not provide guidance or examples of treating any disease or condition that is not associated with inflammation and/or angiogenesis; or what conditions and active agents would be effective in the **prevention** of inflammatory conditions, cancer or hyperproliferative diseases.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the complexity of the inflammatory and angiogenic processes, the cross talk between the two and the necessity to understand the underlying processes associated with various diseases and conditions and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy P. Thomas whose telephone number is (571) 272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TPT/
Timothy P. Thomas
Patent Examiner

Ardin H. Marschel 11/13/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER